Amendments to the Claims

The following amendments replace all prior versions of claims.

1-19. (canceled)

20. (currently amended) ~~The~~ A process ~~of claim 17 further~~ comprising the steps of: (i) contacting a Target Biological Molecule (TBM) having a first and a second site of interest, and containing or modified to contain a nucleophile, selected from the group consisting of thiol, protected thiol, reversible disulfide, hydroxyl, protected hydroxyl, amino, protected amino, carboxyl and protected carboxyl groups, at or near the first site of interest, with a plurality of first organic ligand candidates, said candidates having a functional group reactive with the nucleophile, under conditions such that a reversible covalent bond is formed between the nucleophile and a candidate that has affinity for the first site of interest, to form a TMB-first ligand complex; (ii) identifying the first ligand from the TBM-first ligand complex; (iii) designing a derivative of the first ligand identified in (ii) to provide a small molecule extender (SME) having a first functional group reactive with the nucleophile on the TBM and a second functional group reactive with a second ligand having affinity for the second site of interest, wherein said first functional group is capable of forming an irreversible covalent group with the thiol, protected thiol, reversible disulfide bond, hydroxyl, protected hydroxyl, amino, protected amino, carboxyl or protected carboxyl group on said TBM; (iv) contacting the SME with the TBM to form a TBM-SME complex, and (v) contacting the TBM-SME complex with a plurality of second small organic ligand candidates, said candidates having a functional group reactive with the SME in said TBM-SME complex, wherein a candidate that has affinity for said second site of interest on said TBM forms a reversible covalent bond with said TBM-SME complex, whereby a second ligand is identified.

21. (original) The process of claim 20 wherein the second functional group on said TBM and the functional group on said second ligand candidates in step (v) is a thiol, protected thiol or reversible disulfide group.

22. (original) The process of claim 21 wherein step (v) is conducted under conditions of thiol exchange.

23. (original) The process of claim 22 wherein said conditions are provided by a reducing agent selected from the group consisting of mercaptoethanol, dithiothreitol (DTT), dithioerythreitol (DTE), mercaptopropanoic acid, glutathione, cysteamine, cysteine, tri(carbodiethyl)phosphine (TCEP), and tris(cyanoethyl)phosphine.

24. (original) The process of claim 23 wherein said second ligand candidates in step (v) are members of a library.

25. (original) The process of claim 24 wherein the library member having the highest affinity for said second site of interest on the TBM forms a disulfide bond with the TBM-SME complex.

26-32. (canceled)

33. (currently amended) The ~~method~~ process of claim 20 comprising identifying said second ligand having affinity for said second site of interest on the TBM.

34. (currently amended) The ~~method~~ process of claim 33 wherein said second ligand is identified by mass spectrometry (MS).

35. (currently amended) The ~~method~~ process of claim 33 wherein said second ligand is identified by means of a detectable tag.

36-38. (canceled)

39. (currently amended) The ~~method~~ process of claim 33 ~~or claim 36~~, further comprising the step of synthesizing a molecule comprising said first and second ligands covalently linked to one another.

40. (currently amended) The ~~method~~ process of claim 39 wherein said covalent linkage is provided by a disulfide bond.

41. (currently amended) The ~~method~~ process of claim 40 wherein said molecule consists essentially of said first and second ligands, covalently linked through a disulfide bond.

42. (currently amended) The ~~method~~ process of claim 41 further comprising the step of synthesizing derivatives of said molecule.

43. (currently amended) The ~~method~~ process of claim 42 wherein the disulfide bond covalently linking the first and second ligands is replaced with a different covalent linkage.

44-49. (canceled)

50. (currently amended) A process comprising:

(i) providing a Target Biological Molecule (TBM) containing or modified to contain a reactive nucleophile near a first site of interest on the TBM;

(ii) contacting the TBM from (i) with a small molecule extender having a group reactive with the nucleophile on the TBM and having a free thiol or protected thiol;

(iii) adjusting the conditions of contacting in step (ii) to cause a covalent bond to be formed between the nucleophile on the TBM and the group on the small molecule extender thereby forming a covalent complex comprising the TBM and the small molecule extender, the complex displaying a free thiol or protected thiol near a second site of interest on the TBM;

(iv) contacting the complex from (iii) with a library of small organic molecules each molecule having a free thiol or exchangeable disulfide linking group, under conditions of thiol exchange wherein the library member having the highest affinity for the second site of interest on the TBM forms a disulfide bond with the complex; and

(v) identifying the library member from (iv).

51. (original) The process of claim 50 further comprising the step of synthesizing a molecule consisting essentially of the small molecule extender having the electrophile group from step (ii) covalently linked through the disulfide with the library member identified in step (i).

52. (currently amended) The process of claim 51 further comprising the step of synthesizing a derivative ~~derivatives~~ of the molecule.

53. (original) The process of claim 52 wherein the derivative contains a different group reactive with the nucleophile.

54. (currently amended) The process of claim 52 wherein the disulfide group covalently linking the small molecule extender with the library member identified in step (i) is replaced with a different group.

55. (currently amended) The process of claim 50 further comprising synthesizing a molecule consisting essentially of the small molecule extender without the group reactive with the nucleophile covalently linked through the disulfide with the library member identified in step ~~(e)~~ (v).

56. (currently amended) The process of claim 55 further comprising replacing the disulfide, covalently linking the small molecule extender without the group reactive with the nucleophile with the library member identified in step (c), with a different group.

57. (original) The process of claim 50 wherein the reactive nucleophile is a thiol.

58. (original) The process of claim 57 further comprising, after step (i),

(a) contacting the TBM with a library of small organic molecules, each molecule having an exchangeable disulfide linking group, under conditions of thiol exchange wherein the library member having the highest affinity for the first site of interest forms a disulfide bond with the TBM;

(b) identifying the library member from (i); and

(c) forming a derivative of the library member in (ii) that is the small molecule extender having a group reactive with the nucleophile and having a thiol or protected thiol of step (b).

59. (original) The process of claim 58 further comprising adding a disulfide reducing agent selected from the group consisting of mercaptoethanol, dithiothreitol (DTT), dithioerythreitol (DTE), mercaptopropanoic acid, glutathione, cysteamine cysteine, tri(carboxyethyl)phosphine (TCEP), and tris(cyanoethyl)phosphine.

60-63. (canceled)

64. (original) The process of claim 50 wherein the identifying step comprises mass spectrum analysis.

65. (original) The process of claim 58 wherein the identifying step comprises mass spectrum analysis.

66. (canceled)

67. (original) The process of claim 58 wherein each molecule in the library of small organic molecules having an exchangeable disulfide linking group contains a cysteamine moiety.

68-74. (canceled)